

recited enzymes, the intron by which they are encoded, and references, and in Fig. 6, **which shows the recognition sites for each of the recited enzymes.** No new matter enters by amendment. Upon amendment, claims 38-79 are pending in this application, with claims 38-44 withdrawn from consideration.

Pursuant to the Examiner's request, a clean copy of all pending claims, including new claims 61-79, is attached.

Claims 45-47, 50-54, and 57-60 were rejected under 35 U.S.C. § 112, first paragraph, for allegedly containing subject matter that was not described in the specification in such a way as to reasonably convey to the skilled artisan that the inventors had possession of the claimed invention at the time the application was filed. The Office concedes that the specification discloses endonuclease sites for Class I (I-SceI, I-SceIV, I-PanI) and Class II (I-TevI). However, the Office alleges that the specification fails to disclose any endonuclease sites that represent Class III (I-PpoI), Class IV (I-TevII), and Class V (I-TevIII). The Office contends that, besides Class I I-endonuclease sites (I-SceI, I-SceIV, I-PanI), the specification fails to disclose a representative number of species for Class II I-endonuclease sites, Class III I-endonuclease sites, Class IV I-endonuclease sites, and Class V I-endonuclease sites. The Office concludes that the skilled artisan "would conclude that applicant was not in the possession of the claimed genus because a description of only one member of this genus is not representative of the variants of genus and is insufficient to support the claim." (Paper No. 20 at 4.) Applicants traverse the rejection.

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Since the Office has conceded that that the specification discloses representative endonuclease sites for Class I, the inclusion of claims 47 and 54 in this rejection is in error.

Applicants disagree with the premise on which the rejection is based. Applicants have not described only one member of the claimed genus of Group I intron encoded endonuclease sites. Rather, applicants have described many species that fall within this genus. In Fig. 6, applicants teach the nucleotide sequences of recognition sites for numerous Group I intron encoded endonucleases including I-SceI, I-SceIV, I-SceII, I-Ceul, I-Ppol, I-SceIII, I-Crel, I-Csml, I-Panl, I-TevI, I-TevII, and I-TevIII endonucleases. On page 16, the specification teaches the introns by which I-SceI, I-SceII, I-SceIII, I-SceIV, I-Ceul, I-Crel, I-Ppol, I-TevI, I-TevII, I-TevIII, I-Csml, and I-Panl, endonucleases are encoded, together with references. There can be no doubt that all of these endonuclease sites are Group I intron encoded endonuclease sites. Thus, the Office's premise that applicants have only described one member of the claimed genus of Group I intron encoded endonuclease sites is in error. Also, the Office has provided no reasons why applicants' species of I-SceI, I-SceIV, I-SceII, I-Ceul, I-Ppol, I-SceIII, I-Crel, I-Csml, I-Panl, I-TevI, I-TevII, and I-TevIII endonuclease sites are not representative of all Group I intron encoded endonuclease sites.

Furthermore, on page 17, the specification teaches Classes I-V of Group I intron encoded endonuclease sites and representative members of each group. For example, applicants teach that I-SceI, I-SceII, I-SceIII, I-SceIV, I-Ceul, I-Crel, I-Csml, and I-Panl

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are all Class I sites. The Office has provided no reasons why applicants' species are not representative of all Class I sites. In fact, the Office has conceded that the specification discloses endonuclease sites for Class I and Class II.

In addition, the characteristics of each Class are given. Although Class II, Class IV, and Class V may have no typical structural motifs, they do have characteristics with respect to the site of cleavage, e.g., 4 bp staggered cut with 3' OH overhang, cut internal to recognition site, for Class III. Accordingly, applicants respectfully request withdrawal of the rejection.

Moreover, applicants submit Belfort et al., 1995 (Exhibit 1), as objective evidence that applicants' specification discloses representative species of intron-encoded endonucleases. This publication reviews intron-encoded endonucleases known in 1995, which is after applicants' filing date. (Belfort et al. at 30239, Fig 3.) The paper lists 10 Class I intron-encoded endonucleases (dodecapeptide motif). (*Id.*) Applicants' specification describes 7 of these 10 intron-encoded endonucleases, I-SceI, I-SceII, I-SceIII, I-SceIV, I-CsmI, I-CreI, and I-CeuI. The paper lists 1 Class II intron-encoded endonuclease (GIY-YIG motif), I-TevI. Applicants' specification describes this intron-encoded endonuclease. (*Id.*) The paper lists 3 Class III intron-encoded endonucleases (His-Cys motif). Applicants' specification describes 1 of these 3 intron-encoded endonucleases, I-Ppol. The paper lists 2 Class V intron-encoded endonucleases (H-N-H motif). (*Id.*) Applicants' specification describes 1 of these 2 intron-encoded

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endonucleases, I-TevIII. Overall, applicants' specification describes 10 of the 16 intron-encoded endonucleases described in the paper.

Applicants further provide Turmel et al., 1997 (Exhibit 2), as objective evidence that I-TevII is an intron-encoded endonuclease. (Turmel et al. at 2610, second column, first complete paragraph.) Although other intron-encoded endonucleases have been identified since applicants' application was filed, it is apparent that applicants' specification describes representative species of intron-encoded endonucleases, as well as representative species of each of Classes I through V intron-encoded endonucleases. Accordingly, applicants respectfully request withdrawal of the rejection.

Furthermore, applicants' new claims 61-79 recite specific Group I intron encoded endonuclease sites, the recognition sequences of which are shown in Fig. 6 of the specification. Accordingly, this rejection is inapplicable to new claims 61-79.

Claims 45-60 were rejected under 35 U.S.C. § 112, first paragraph, for allegedly not reasonably providing enablement for any and all Group I intron encoded endonuclease sites. The Office concedes that the specification is enabling for an endonuclease site selected from Class I I-endonuclease sites, wherein the Class I I-endonuclease site is selected from I-SceI, I-SceIV, and I-Panl sites. (Paper No. 20 at 4.) However, the Office alleges that the specification only discloses endonuclease sites for Class I (I-SceI, I-SceIV, and I-Panl) and Class II (I-TevI), but fails to disclose any nucleotide sequences for Class III (I-Ppol), Class IV (I-TevII), and Class V (I-TevIII).

The Office concludes that the skilled artisan "at the time of filing would be unable to use

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the claimed invention, without an excessive and undue amount of experimentation." (Paper No. 20 at 5.) Applicants traverse the rejection.

Since the Office has conceded that that the specification discloses endonuclease sites for Class I (I-SceI, I-SceIV, and I-Panl ), the inclusion of claims 49 and 56 in this rejection is in error. Similarly, since the recognition sequence for Csml is taught in Fig. 6 of the specification, claims 48 and 55, which recite I-SceI, I-SceIV, Csml, and I-Panl, should not be included in this rejection.

Applicants disagree with the Office's allegation that the specification only discloses endonuclease sites for Class I (I-SceI, I-SceIV, and I-Panl ) and Class II (I-TevI). In Fig. 6, applicants teach the nucleotide sequences of recognition sites for numerous Group I intron encoded endonucleases including I-SceI, I-SceIV, I-SceII, I-Ceul, I-Ppol, I-SceIII, I-Crel, I-Csml, I-Panl, I-TevI, I-TevII, and I-TevIII endonucleases. There can be no doubt that the specification discloses numerous Group I intron encoded endonuclease sites, including Class III (I-Ppol), Class IV (I-TevII), and Class V (I-TevIII) endonuclease sites. Consequently, the premise on which the Office's rejection is based is in error. Accordingly, applicants respectfully request withdrawal of the rejection.

Furthermore, applicants are not required to disclose every species encompassed by their claims. *In re Angstadt*, 537 F.2d 498, 502-503, 190 U.S.P.Q. 214, 218 (C.C.P.A. 1976). As in *Angstadt*, applicants have provided numerous working examples. See *id.* Applicants submit that, as in *Angstadt*, 35 U.S.C. § 112, first

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paragraph, does not require applicants to disclose every Group I intron encoded endonuclease site capable of working in the claimed invention.

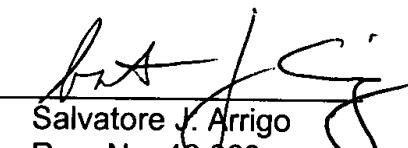
Applicants new claims 61-79 recite specific Group I intron encoded endonuclease sites, the recognition sequences of which are shown in Fig. 6 of the specification. Accordingly, this rejection is inapplicable to new claims 61-79.

Applicants respectfully submit that the application is in condition for allowance, and respectfully request issuance of a notice of allowance. If the Examiner should disagree, he is invited to contact the undersigned to discuss any remaining issues.

Please grant any extensions of time required to enter this response and charge any additional required fees to our deposit account 06-0916.

Respectfully submitted,

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